

RING EXPANSION OF 3-SUBSTITUTED 1,2-BENZOISOTHIAZOLE 1,1-DIOXIDES  
TO 1,2-BENZOTHIAZEPINE 1,1-DIOXIDES

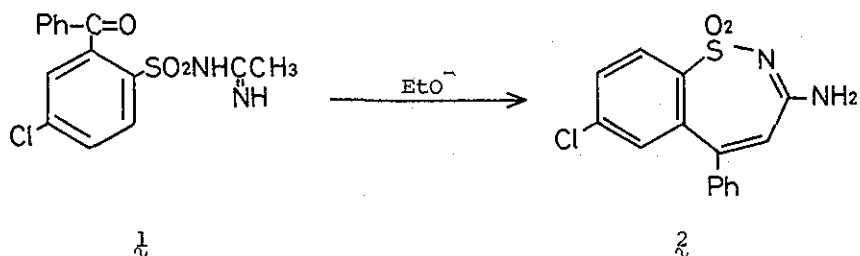
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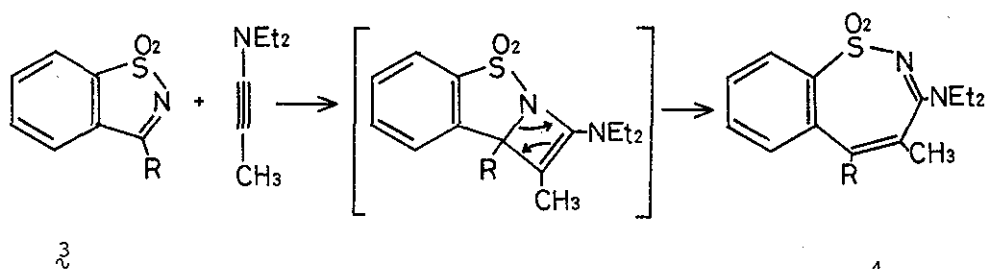
3-Substituted 1,2-benzisothiazole 1,1-dioxides undergo a [2+2]cycloaddition with 1-diethylaminopropyne followed by ring expansion to give the very stable 5-substituted 3-diethylamino-4-methylbenzo-1,2-thiazepine 1,1-dioxides (4). These can, however, be cleaved with lithium aluminum hydride to o-styryl-sulfonamides. The stability of the ring system 4 is discussed briefly.

There has been only one report of the synthesis of a 1,2-benzothiazepine 1,1-dioxide, namely the cyclization of the o-benzoylbenzenesulfonylamidine derivative 1 to 2.<sup>1</sup> The compound was reported to have hypotensive and diuretic

activity. No other aromatic 1,2-benzothiazepines have been described. We now report a simple general two step synthesis of this ring system from saccharin by the ring expansion of the readily available 3-substituted 1,2-benzoisothiazole 1,1-dioxides (3).<sup>2</sup>

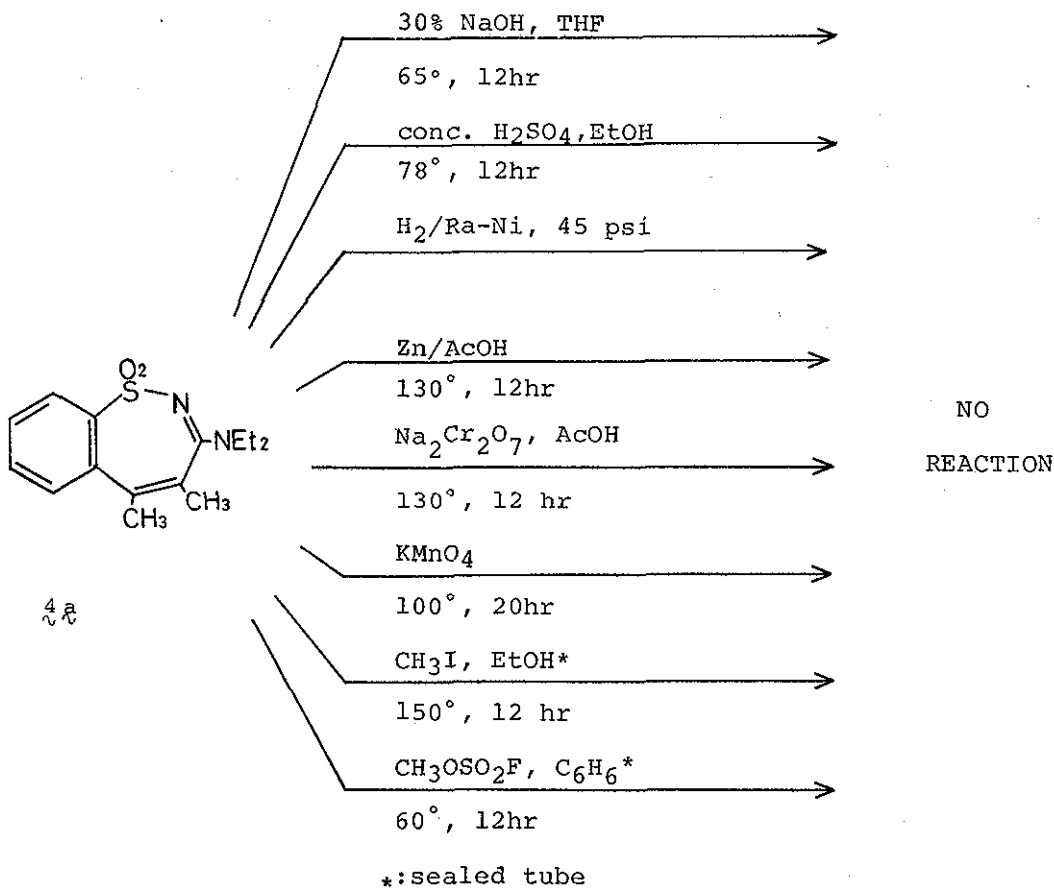


Addition of 1-diethylaminopropyne to **3** in acetonitrile at room temperature<sup>3</sup> gave the 5-substituted 3-diethylamino-4-methylbenzo-1,2-thiazepine 1,1-dioxides (**4**) in good yield. The [2+2] cycloadditions of ynamines with imines,<sup>4</sup> olefins,<sup>5</sup> and aldehydes and ketones<sup>4</sup> are well known and it is assumed that a similar addition takes place with **3** followed by ring-expansion:



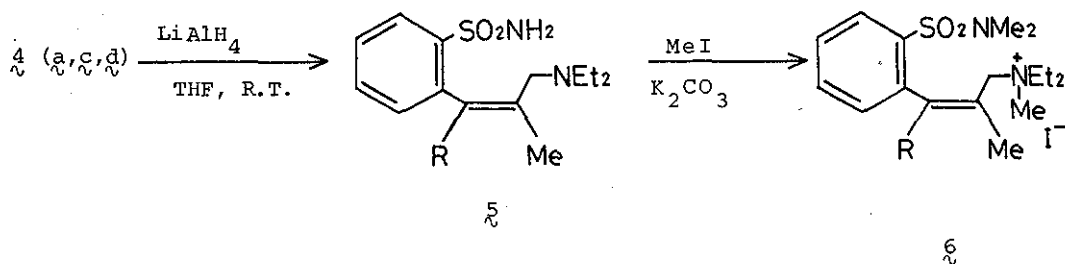
- 4**
- a: R=CH<sub>3</sub>; mp 154°
  - b: R=C<sub>2</sub>H<sub>5</sub>; mp 110°
  - c: R=Ph; mp 195°
  - d: R=OEt; mp 145°
  - e: R=SMe; mp 125°

The structural assignment of  $4$  was consistent with its spectral properties. For example, when  $R=CH_3$  in  $4$ , the compound showed the presence of a  $C=N$ -bond ( $1620\text{ cm}^{-1}$ ) and a sulfonyl group ( $1300, 1160\text{ cm}^{-1}$ ) in the infrared, two methyl singlets ( $\delta$  3.22 and 3.12), a 4 H doublet of quartets at  $\delta$  3.43 due to the methylene protons in  $(Et)_2$ , and a 6 H doublet of triplets for the two methyl groups in  $(Et)_2$ . The mass spectrum also supported structure  $4$ . Thus, loss of  $SO_2$  resulted in the formation of a 2-diethylaminoquinolinium ion ( $m/e$  228) and a number of important fragments, including the base peak ( $m/e$  157), could be assigned quinolinium ion structures.



Scheme

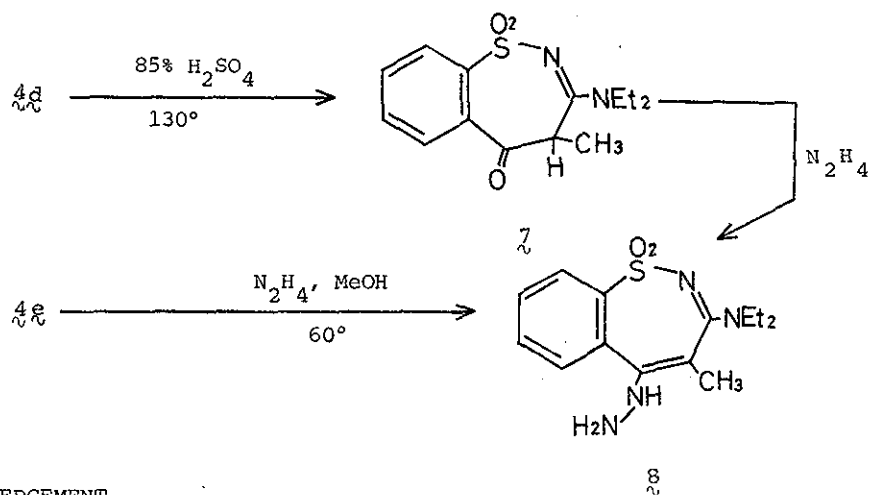
On the other hand, this ring system is remarkably stable to a wide variety of chemical reagents (Scheme), which is reminiscent of compounds exhibiting 'aromatic' stability. It could be cleaved, however, with lithium aluminum hydride in tetrahydrofuran at room temperature to give the *o*-styryl-sulfonamide (**5**) which, on treatment with an excess of methyl iodide in the presence of potassium carbonate, gave the quaternary salt **6**. The nmr spectra of **5** and **6** agree with the proposed structures and hence support the structure



of **4**. Thus, **5** (R=Ph) exhibits a methylene singlet at  $\delta$  3.0, a methyl singlet at  $\delta$  2.0, two *N*-ethyl groups and an  $\text{NH}_2$  singlet ( $\delta$  4.80, exchangeable). The mass spectral fragmentations correspond to loss of  $-\text{SO}_2\text{NH}_2$  ( $m/e$  280), loss of  $-\text{CH}_2\text{NEt}_2$  ( $m/e$  272), and loss of the whole vinyl side chain ( $m/e$  165). **6** (R=Ph) also exhibits a methylene singlet ( $\delta$  4.0), two *N*-Me singlets ( $\delta$  2.8), an  $\text{NMe}^+$  singlet ( $\delta$  3.2), an allylic methyl ( $\delta$  2.2), and the  $\text{NEt}_2$  group.

When **4** (R=OEt; colorless) was heated with 85%  $\text{H}_2\text{SO}_4$  at  $130^\circ$  the ketone (**7**) mp  $185^\circ$  was formed [ $\gamma_{\text{C=O}}$   $1685 \text{ cm}^{-1}$ ; Me doublet at  $\delta$  1.90 ( $J \approx 6.0 \text{ Hz}$ )] which with hydrazine gave the hydrazine (**8**), mp  $137^\circ$  (rather than the hydrazone) (3 exchangeable H with  $\text{D}_2\text{O}$ , Me singlet at  $\delta$  1.85). The same hydrazine was obtained by heating **4** (R=SMe, red) with hydrazine in methanol

at 60°. That  $\zeta$  exists exclusively in the ene-hydrazine rather than hydrazone form again speaks for the 'aromatic character' of this 1,2-thiazepine 1,1-dioxide system.



#### ACKNOWLEDGEMENT

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#### REFERENCES

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3. When R=OEt, much more vigorous (180°, sealed tube) conditions had to be used, but R=SMe reacted normally at room temperature.
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